RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)									DATE February 1999	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 1							R-1 ITEM NOMENCLATURE In-House Laboratory Independent Research (ILIR) PE 0601101D8Z			
COST*(In Millions)*	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
Total Program Element (PE) Cost	1.495	2.167	2.033	2.021	2.102	2.099	2.143	2.188	Continuing	Continuing
ILIR/P503	1.495	2.167	2.033	2.021	2.102	2.099	2.143	2.188	Continuing	Continuing

(U) A. Mission Description and Budget Item Justification

(U) BRIEF DESCRIPTION OF ELEMENT

(U) This program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS) and provides the only programmed research funds received by the University. This program facilitates the recruitment and retention of faculty, supports state-of-the-art capabilities for training military medical students, and allows the collection of pilot data by the University's faculty researchers. Pilot data allow the faculty to secure research funds from non-DoD sources (est. $20-$25 million annually). Approximately 80 to 100 intramural research projects (20-25 new starts) are awarded each year, on a peer-reviewed, competitive basis. Results from these studies contribute to the fund of knowledge intended to enable technical approaches and investment strategies within Defense science and technology (S&T) programs.

(U) The ILIR program at USUHS is designed to answer fundamental questions of importance to the military medical mission of the Department of Defense in the areas of Combat Casualty Care (CCC), Infectious Diseases (ID), Military Operational Medicine (MOM), and Nuclear, Biological and Chemical (NBC) Medical Defense. The port folio of research projects will vary annually because this research is investigator-initiated. Examples of typical research efforts are:

- Combat Casualty Care: ischemia and reperfusion injury, traumatic brain and peripheral nerve injury, cryopreservation and substitution of blood components, endotoxic shock, inflammation and wound healing.

- Infectious Diseases: immunology and molecular biology of bacterial, viral and parasitic disease threats to military operations. These threats include *E. coli* and their shiga toxins, gonorrhea, streptococcus, hepatitis A, Venezuelan equine encephalitis (VEE), malaria, and bartonellosis.

- Military Operational Medicine: military and medical training and readiness.

- Nuclear, Biological and Chemical Defense: basic research questions concerning nerve agent intoxication and treatment.

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(U) Project Number and Title: P503 ILIR

(U) PROGRAM ACCOMPLISHMENTS AND PLANS

(U) FY1998 Accomplishments:

(U) Combat Casualty Care: This program supported 24 projects in Combat Casualty Care. The following are examples of the objectives of a few highlighted protocols: a) Investigate the vascular effects of biochemicals that cause inflammation related to wounding and wound healing; b) Continue the investigation of the role of endotoxin, the lipopolysaccharide outer membrane component of gram negative bacteria leading to multiorgan failure, shock, and death; c) Study the molecular events underlying muopioid receptor activation to develop better pain relief strategies; d) Examine the effects of neurocytokines, biochemicals that are released upon nerve damage, in peripheral nerve and brain injury; e) Investigate healing mechanisms following ischemia-reperfusion injury; f) develop a blood test for diagnosing malignant hyperthermia susceptibility for use on the battlefield. ($ 0.519 Million)

(U) Infectious Diseases: Twenty-six projects addressing basic research questions in Infectious Diseases were funded for FY1998. Highlights from the plans of these projects include: a) Continue the investigation of Venezuelan equine encephalitis (VEE) by examining the role of macrophages and cytokines in the early immune response and development of inflammation of the central nervous system; b) Continue to investigate how environmental regulation of gonoccocal gene expression plays a critical role in the pathogenesis of the sexually transmitted disease *N. gonorrhoeae*; c) Develop a small animal model to determine the molecular mechanisms and regulation of *Salmonella typhi* invasion of epithelial cells; d) Determine the chronic infection rate, disease burden, risk factors within a population endemic for *B. Bacilliformis* (Batonellosis); e) Study the gene regulation of the shiga-like toxins coming from enterohemorrhagic *Escherichia coli*; f) Continue data collection for the comparison of two inactivated hepatitis A vaccines for their cross-immunogenicity and efficacy.
($ 0.572 Million)

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(U) **Military Operational Medicine:** FY1998 funds supported 23 projects in Military Operational Medicine. Goals of a few representative proposals are as follows: a) Investigate psychobiological dysfunction (PTSD symptomology) resulting from exposure to combat-like trauma; b) Understand how stress-induced changes in glucocorticoid hormones suppress the immune response; c) Continue to investigate the training practices impacting exertional heat illness in Marine Corps basic training, as well as to study how immune function is affected by exercise; d) Attempt to determine the relationship of health outcomes and job performance to substance use in the military; e) Delineate the gene transcription mechanisms underlying neural enhancement of cognitive function and soldier performance; f) Continue work to understand chronobiotic role of extra-retinal light reception in the control of the physiologic circadian rhythm. ($ 0.264 Million)

(U) **Nuclear, Biological and Chemical Medical Defense:** There were six projects in progress in FY1998 in the NBC area. Representative research efforts in this area are: a) Characterize the breakdown of 1,4-benzodiazepines, such as valium, used as an antidote to central nervous system effects of nerve agent poisoning; b) Study the pattern of sensory input to the frontal cortex for treatment of head injury; c) Study the DNA structure and repair mechanisms of the organism *Deinococcus radiodurans* to understand the mechanism of its extraordinary resistance to radiation; d) Study the functional deficits induced by neocortical cholinergic depletion and the potential restoration of function by administration of nerve growth factor. ($ 0.14 Million)

(U) **FY1999 Plans:**

(U) **Combat Casualty Care:** The objective of this program is to provide support for a significant number of new and continuing projects in Combat Casualty Care from FY1998. The program is continuing to investigate various aspects of wounding and wound healing and the roles that inflammatory mediators play in these processes. Projects to elucidate cellular and molecular mechanisms in endotoxic shock and its treatment continue to be an important area of research. Another major thrust area is peripheral nerve injury and traumatic brain injury with the use of animal models and nerve cells in culture. Included in this program is the investigation of low power laser therapy to decrease programmed cell death when motor nerves are severed. ($ 0.82 Million)

(U) **Infectious Diseases:** This broad area continues to be one of emphasis within the USUHS; approximately 30 protocols are supported in this area. Militarily relevant bacterial threat agents such as *E. coli* and its toxins, gonococcus, and streptococcus garner significant available resources. Mobilization of macrophages and antibody production continues to be studied within the context of Venezuelan equine encephalitis. The initiative to study typhoid fever with the development of an animal model continues. Research continues the study of bartonellosis in Peru by examining the vector and the animal reservoir, and by performing studies of the epidemiology of this parasitic disease. The study of the comparison of two inactivated hepatitis A vaccines should be brought to completion with the final results influencing the decision for vaccination of military personnel. ($ 0.739 Million)

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(U) **Military Operational Medicine:** FY1999 funds are supporting research in training and military readiness as a critical area within Military Operational Medicine. Training practices and their effects on exertional heat illness of Marine Corps basic training recruits continue to be examined, as well as the study of the effects of exercise and exertion on the immune system. Studies to determine the effects of stress and nicotine intake and dysfunctional eating habits also continue. New work to delineate neural mechanisms underlying post-traumatic stress disorder (PTSD) is being initiated. Other studies addressing different aspects of military training and readiness are anticipated. ($ 0.391 Million)

(U) **Nuclear, Biological and Chemical Medical Defense:** Multiple basic research projects in this threat area are being supported. Analysis of the chemical breakdown of different isomers of 1,4 benzodiazepines, such as Valium, and other chiral drugs used as antidote to central nervous system effects of nerve agent poisoning, continue. Study of the pattern of sensory input to the frontal cortex is being supported. The organism that exhibits extraordinary resistance to ionizing radiation, *Deinococcus radiodurans*, is being examined to better understand what gives it this unique ability. A study is being initiated to study the role of mitochondrial membrane proteins in agent-induced cell death.($ 0.217 Million)

(U) **FY2000 Plans:**

(U) Efforts will continue in all the major research areas (CCC, ID, MOM, and NBC) for FY2000. Specific projects compete for funding each year, therefore, detailed description of the research is impossible at this time. ($ 2.033 Million)

(U) **FY2001 Plans:**

(U) Efforts will continue in all the major research areas (CCC, ID, MOM, and NBC) for FY2001. Specific projects compete for funding each year, therefore, detailed description of the research is impossible at this time. ($ 2.021 Million)

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(U) B. Program Change Summary	FY1998	FY1999	FY2000	FY2001	Total Cost
Previous Presidents Budget	1.513	2.173	2.068	2.057	Continuing
Appropriated Value	1.569	0	0	0	Continuing
Adjustments to Appropriated Value					
a. Congressionally Directed Undistributed Reduction	-0.074	-0.006			
b. Rescission/Below-threshold Reprogramming, Inflation Adjustment	0	0	-0.035	-0.036	
c. Other	0	0			
Current Presidents Budget	1.495	2.167	2.033	2.021	Continuing

Change Summary Explanation: Funding changes are due to congressional undistributed reductions and inflation adjustments.

(U) Funding: N/A

(U) Schedule: N/A

(U) Technical: N/A

(U) C. OTHER PROGRAM FUNDING SUMMARY COST: N/A

(U) D. ACQUISITION STRATEGY: N/A

(U) E. SCHEDULE PROFILE: N/A